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Research Article

Spray Gel Formulation of Goroho Banana (*Musa acuminata* L.) Peel Extract: Optimization and Wound Healing Activity Analysis

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ABSTRACT

Goroho banana (*Musa acuminata* L.) peel extract has been traditionally used in Minahasa for wound healing. This study aimed to develop and optimize a spray gel formulation containing Goroho banana peel extract and evaluate its wound healing activity. A factorial design was employed with two factors (Carbopol 940 and HPMC) at two levels. Preliminary testing determined 3% as the optimal extract concentration through wound healing evaluation in rats. Four spray gel formulations were developed and characterized for physicochemical properties, including viscosity, pH, and drying time. Results showed Formula B (Carbopol 0.5% and HPMC 0.6%) exhibited optimal characteristics with viscosity 223.8 ± 7.6 cPs, pH 5.13 ± 0.05, and drying time 4.22 ± 0.05 minutes. The HET-CAM irritation test revealed mild irritation scores (2.5-3.8) for all formulations, with Formula B showing the lowest score (2.5). Design Expert optimization generated 100 solutions, with the optimal formula containing Carbopol 0.670% and HPMC 0.517%. The wound healing activity showed no significant differences between spray gel formulations and Bioplacenton ($p>0.05$), indicating comparable efficacy. This study demonstrates the successful development of a safe and effective spray gel formulation of Goroho banana peel extract for wound healing applications.

INTRODUCTION

With around 80% of the world's population depending on natural or "back to nature" products, the growing popularity of herbal treatment has spread throughout the globe (Ekor, 2014). This trend is noticeable in Indonesia, where traditional herbal medicine still plays a big part in healthcare procedures (Adiyasa and Meiyanti, 2021). Despite the general perception that herbal treatments are effective and have few adverse effects, scientific investigation indicates that there is a risk of toxicity because of our incomplete knowledge and how they interact (Arimbawa, 2022).

This research aims to investigate the wound-healing potential of Goroho banana (*Musa acuminata* L.) peel extract in a spray gel formulation, focusing on its physicochemical properties and wound treatment capabilities. The present research aims to address the information deficit in the scientific investigation of endemic North Sulawesi plant resources and their potential for the development of natural herbal therapeutic products.

Existing research has demonstrated the diverse therapeutic properties of herbal medicines, ranging from analgesic and anticancer to antioxidant and antibacterial applications (Ekayanti, 2023; Nursanty and Zumaidar, 2009; Saefudin *et al*., 2013; Witantri, 2015). Wound healing, in particular, represents a critical area of medical intervention, where the risk of bacterial infection poses significant challenges (Ernst, 2007; Qomariah *et al*., 2014). Traditional practices in the Minahasa region have historically used various plant parts, including the Goroho banana skin and leaves, for wound treatment through empirical methods (Pareda *et al*., 2019).

The development of wound dressing

products containing herbal antibacterial agents has gained significant attention, with various formulations including liquids, salves, and bandages (Shiffman and Low, 2021). Spray gel formulations provide distinct benefits, including minimizing direct contact with wounds and reducing potential contamination (Nurmalasari *et al*., 2017). The potential of herbal plant extracts in wound healing includes enhancing blood clotting, combating infection, and accelerating wound recovery (Thakur *et al*., 2011).

Preliminary studies have shown promising antibacterial potential across different parts of the Goroho banana plant (Rante *et al*., 2017). Kurniawan *et al*. (2013) previously found bioactive components, including flavonoids, saponins, tannins, in banana peels (Kurniawan *et al*., 2013). However, there has been little through scientific research on how effective the extract from Goroho banana peels is for healing wounds, both in lab tests (in vitro) and in living (in vivo) organisms.

The novelty of this research lies in its innovative approach to developing a spray gel wound dressing utilizing local plant resources. This research looks at how to use traditional knowledge and modern methods to see if the extract from Goroho banana (*Musa acuminata* L.) (*Musa acuminata*) peels can work as a natural antibacterial agent. Moreover, this research will optimize the spray gel composition using components including carbopol, hydroxypropyl methylcellulose (HPMC), propylene glycol, and other excipients to enhance wound healing properties.

This research contributes to the growing body of knowledge on indigenous plant resources, offering a scientific foundation for developing natural, locally sourced herbal medicinal products. By leveraging the rich biodiversity of North Sulawesi and applying rigorous scientific methodologies, the study seeks to validate traditional healing practices and unlock the potential of endemic plant species in modern healthcare applications.

METHODS

This experimental laboratory study was conducted at the Pharmacy Laboratory of Prisma University Manado for extraction, spray gel formulation, and wound healing activity tests. The ethical clearance was obtained from the Ethics Committee of Medicine, Udayana University (No. B/164/UN14.2.9/PT.01.04/2024).

Materials

The main material used was Goroho banana peel *(Musa acuminata L.)* collected from Koka Village, Tombulu District, Minahasa Regency. Other materials included carbopol 940, triethylene glycol (TEA), HPMC, propylene glycol, methylparaben, ethanol 96%, and distilled water.

Instrumentation

The instruments used included glassware, a caliper, filter paper, spray bottles, an oven, a pH meter, a rotary evaporator, an analytical balance, biopsy punch, and an Ostwald viscometer.

Extraction

The Goroho banana peels were cleaned under running water, drained, chopped, and dried at room temperature. The dried samples were ground and sieved to obtain simplices powder. The extraction was performed by maceration method using 96% ethanol for 5 days to obtain filtrate 1 and residue 1. The residue was re-macerated for 3 days to obtain filtrate 2. Both filtrates were combined and evaporated using an oven until a thick extract was obtained.

Gel Base Preparation

Carbopol 940 is added to distilled water until dispersed and homogeneous in a mortar until a gel base is formed. TEA is added gradually to neutralize the gel base and also increase the viscosity of the gel.

Preliminary Test Animal Treatment

The purpose of conducting an excision wound healing effectiveness test in the preliminary study is to obtain the optimal concentration of Goroho banana peel extract in the spray gel. A total of 25 healthy male white rats with an average weight of 200 grams were used. The back of the rats was shaved to approximately 5 cm and then anesthetized using ketamine. The back area was cleaned using povidone iodine and then 70% alcohol. Subsequently rat wounds were exposed by excision using a sterile biopsy punch with a wound depth of approximately 0.5 – 1 mm and a wound diameter of approximately 4 mm. The study was conducted in 5 groups with randomly selected animals, with each group containing 5 rats. Biopsy wound treatment was performed by applying gel extract of Goroho banana peel to the rats' backs using a cotton bud, applied once daily during the day time.

Wound contraction was measured using a caliper on days 1, 3, 6, 9, and 12. Wound contraction was calculated using the formula :

$$\text{Wound contraction (\%)} = \frac{(\text{Initial wound length} - \text{Wound length on day n})}{\text{Initial wound length}}$$

The spray gel formulations were evaluated from organoleptic properties, homogeneity, pH, viscosity, spreadability, spray pattern, and drying time according to standard procedures.

Evaluation of Spray Gel Preparation
Organoleptic

This test is conducted to observe the physical appearance of the preparation visually by examining the smell, color and texture of the spray gel preparation (Zubaydah, 2022). This test needs to be carried out to determine whether changes occur or not (Zubaydah *et al*., 2022).

Homogeneity

The homogeneity test is conducted to observe the presence or absence of solid particles or gel-forming agents that are still clumping in the spray gel preparation. The standard for spray gel preparations must be homogeneous, indicating that the formulated preparation is homogeneous or well-mixed so that the preparation can be evenly distributed when applied (Zubaydah *et al*., 2022).

pH

The pH test is conducted to assess the acidity level of the preparation to ensure that the Spray gel preparation does not cause skin irritation. Ideally, topical preparations should have a pH value similar to skin pH, which ranges from 5-7 (38). Research conducted by Sim *et al.* (2022) stated that pH has been proven to play a role in mediating wound healing rate, where pH 4 was observed to stimulate faster wound healing (Sim *et al.*, 2022).

Viscosity

Viscosity test is a liquid property related to flow resistance. Viscosity is defined as the force required to move a flat surface past another flat surface. The viscosity standard in spray gel preparation ranges from 200-300 cPs (Zubaydah, 2022).

Spray Pattern Test

The spray pattern test is conducted to observe the pattern of spray formation. A good spray pattern is observed when the sprayed preparation functions and particles are small and evenly distributed. This test is usually performed by spraying on a plastic sheet, then numbering at certain distances, followed by spraying in duplicate at each distance (Zubaydah, 2022).

Drying Time

Drying time is the time required for the spray gel preparation to dry by spraying the preparation on powder paper. The calculation is done using a stopwatch, with the required drying time for spray gel preparations being less than 5 minutes (Sumardiko *et al*., 2023).

Adhesiveness

The adhesion test is performed by spraying the preparation onto the upper arm skin from a 3 cm distance. During a 10-second observation period, the test evaluates whether the formulation effectively adheres to the skin surface or if droplets will flow downward, assessing the product's ability to remain in place after application (Anindhita and Oktaviani, 2020).

Irritation Testing

Irritation testing was conducted using the Hen's Egg Test Chorioallantoic Membrane (HET-CAM) method. Fertilized chicken eggs (*Ovum gallus domesticus*) were incubated at 37^{o}C and rotated for 10 days. On the 10th day, eggs were candled to confirm the presence of living embryos, with unfertilized eggs or those without living embryos were discarded. The egg's air sac was marked and then opened by carefully removing the outer shell using sterile scissors. To facilitate this process, the shell was softened using warm 0.9% NaCl solution and re-incubated for 5-20 minutes to allow easy removal of the outer membrane. Eggs with damaged CAM during the process were excluded from testing. A total of 300 mg of sample, including 45% lactic acid solution as a positive control, distilled water as a negative control, and spray gel extracts of Goroho banana peel (formulas 1, A, B, and AB) were applied to the CAM and subsequently observed for 300 seconds to asses hemorrhage, lysis and coagulation (Yuliani *et al.*, 2017).

The spray gel preparations of Goroho banana peel that underwent HET-CAM irritation testing were subsequently scored for hemorrhage, lysis, coagulation, and edema using the following equation:

$$T = \frac{301 - H}{300} x\, 5 + \frac{301 - L}{300} x\, 7 + \frac{301 - C}{300} x\, 9$$

Where:
T= irritation score
H= time required to induce hemorrhage (seconds)
L= time required to induce lysis (seconds)
C= Time required to induce coagulation (seconds)

The results obtained from calculations were then compared with the following Table 1.

Data Analysis

The analyzed parameters included pH, spreadability, viscosity, and drying time, which were evaluated using factorial design calculations through Design Expert software version 13. This analysis enabled the assessment of the effects of gelling agents (Carbopol and HPMC), their interactions, and the identification of factors that significantly influenced the response variables such as pH, viscosity, and drying time, ultimately determining the optimal composition of the tested gel formulation. For wound healing activity assessment, SPSS 25 version and R studio were employed to evaluate significant changes in incision wounds when treated with either the extract or the spray gel formulation.

RESULTS AND DISCUSSION

Extraction

The process of extracting Goroho banana peel *(Musa acuminata L.)* involved several steps of preparation and extraction. The dried simplices of Goroho banana peel initially weighed 1,148 g, from which 93.9 g of extract was obtained, resulting in an extraction yield of approximately 8.18%. The extraction process utilized maceration techniques with an appropriate solvent system, which effectively isolated the bioactive compounds from the banana peels. The relatively moderate extraction yield of 8.18% suggests the presence of specific phytochemical components that were successfully extracted from the plant material.

The yield percentage is consistent with typical extraction processes for plant materials. Extraction efficiencies can vary depending on multiple factors including solvent polarity, extraction method, drying and preprocessing of plant material, and specific characteristics of the plant species.

Preliminary Test

A preliminary test was conducted to determine the optimal concentration of Goroho banana peel extract in the excision wound healing process on white Wistar rats. The research employed a gel formulation of carbopol and TEA combined with extract at different concentrations (1%, 3%, and 5%), using Bioplacenton as a positive control and gel base without extract as a negative control.

Table 1. HET-CAM irritation score indicators

No.	HET-CAM Irritation Score	Response Category
1	≤ 0.9	Negligible
2	1.0 – 4.9	Slight Irritation
3	5.0 – 8.9	Moderate Irritation
4	9.0 – 21	Severe Irritation

Table 2. The average of wound healing with STD.

Group	The Average of Wound Healing Day -				
	1	3	6	9	12
Bioplacenton	3.92 ± 0.08	3.52 ± 0.17	2.5 ± 0.5	1.18 ± 0.44	0.75 ± 0.3
Gel base	4 ± 0	3.94 ± 0.08	3.38 ± 0.59	2.02 ± 1.19	1.1 ± 0.15
1%	3.91 ± 0.13	3.41 ± 0.19	2.04 ± 0.17	1.22 ± 0.16	0.76 ± 0.08
3%	3.98 ± 3.66	3.66 ± 0.1	2.73 ± 0.1	1.34 ± 0.28	0.73 ± 0.06
5%	3.98 ± 0.03	3.59 ± 0.13	2.98 ± 0.06	1.53 ± 0.3	0.99 ± 0.11

*average±STD, standard deviation.

Table 3. The percentage of wound healing with STD.

Group	The Percentage (%) of Wound Healing Day -				
	1	3	6	9	12
Bioplacenton	32 ± 1.9	12 ± 4.01	37.5 ± 16.2	70.5 ± 11.2	81.75 ± 7.3
Gel base	0 ± 0	1.5 ± 0.08	15.5 ± 14.8	49.5 ± 4.9	72.5 ± 3.95
1%	2.25 ± 0.13	14.7 ± 4.62	49 ± 4.28	69.4 ± 4.2	81 ± 2.23
3%	0.5 ± 0,68	8.5 ± 2.4	31.75 ± 2.6	66.27 ± 7.2	81.75 ± 1.43
5%	0.5 ± 0.6	10.2 ± 3.35	25.5 ± 1.4	61.75 ± 7.4	75.25 ± 2.7

*percentage±STD, standard deviation.

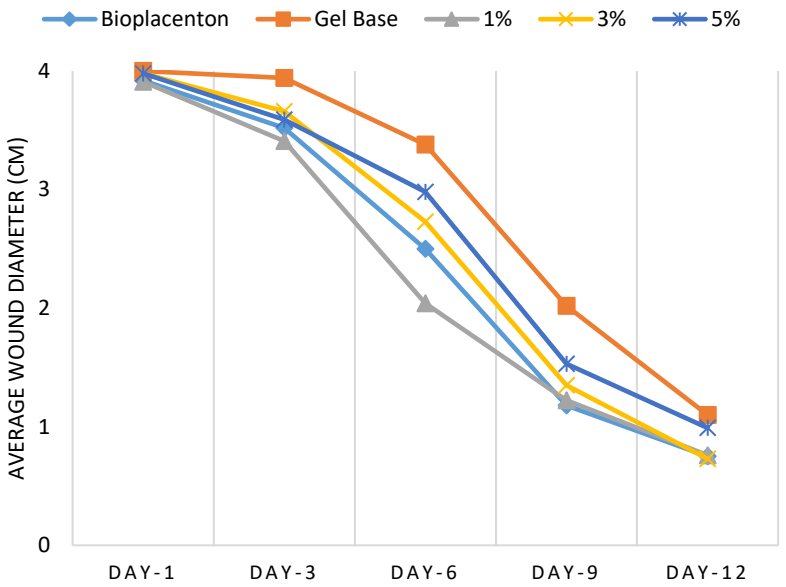

Figure 1. Graph of Rat Excision Wound Area. There were significant differences on days 3, 6, 9 and 12.

Data analysis began with the normality testing of wound measurements on days 1, 3, 6, 9, and 12, which revealed a non-normal distribution. Subsequently, the Kruskal-Wallis test was performed, demonstrating significant differences among the six treatment groups ($p<0.05$). Further analysis using the Mann-Whitney Post Hoc test revealed significant differences in wound healing progression on days 3, 6, 9, and 12. (Figure 1).

Mann-Whitney post hoc analysis revealed significant differences ($p<0.05$) between all treatment groups, particularly on days 3 and 6. The research revealed interesting wound-healing dynamics in each treatment group. The positive control group showed consistent wound diameter reduction, from 3.92 cm on the first day to 0.75 cm on day 12. In contrast, the negative control group exhibited a slower healing progression, with wound diameter reducing from 4 cm to 1.1 cm by day 12.

Groups with varying extract concentrations displayed an intriguing pattern of wound diameter reduction. Increased extract concentrations were associated with accelerated wound healing. The 5% concentration group showed the most rapid initial healing, reaching a diameter of 0.99 cm by day 12. However, a deeper analysis indicated that the 3% concentration appeared to be the most optimal formulation. On day 12, this group's wound diameter reached 0.73 cm, the smallest of all groups. While the 5% group demonstrated faster

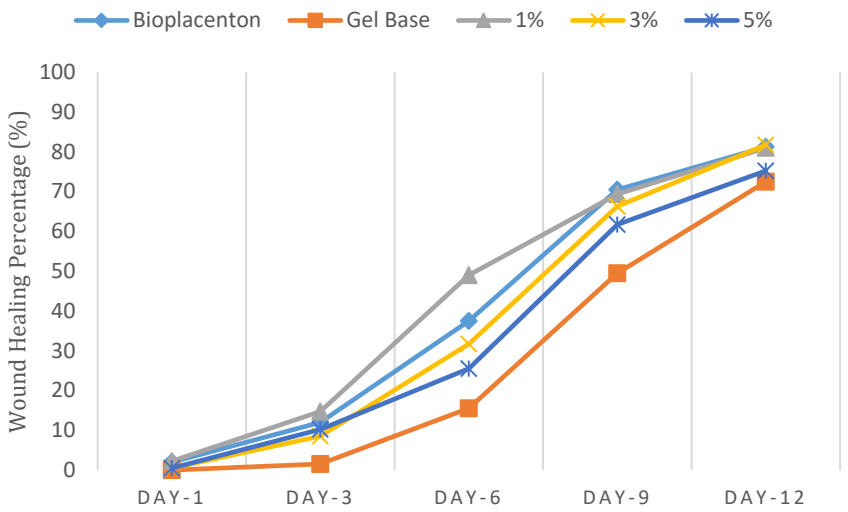

Figure 2. Graph of Wound Healing Percentage. There were significant differences on days 3, 6, 9 and 12.

faster initial healing, the 3% group showed the best overall wound closure during the research.

The significant wound healing properties of Goroho banana peel can be attributed to its bioactive compounds, including flavonoids, saponins, and tannins, which exhibit anti-inflammatory, antioxidant, and antimicrobial activities essential for wound healing (Pangemanan *et al*., 2020). These compounds, particularly tannins and flavonoids, effectively reduce wound inflammation and prevent further tissue damage by neutralizing free radicals (Rizka *et al*., 2023). Studies have demonstrated that Goroho banana peel extract accelerates fibroblast proliferation, crucial for new tissue formation during wound healing, thereby enhancing re-epithelialization and improving the strength of newly formed skin (Rifasanto *et al*., 2018). The ethanol extract shows significant antibacterial activity against Staphylococcus aureus, a common wound pathogen, thus preventing infection during the healing process (Pangemanan *et al*., 2020). Animal studies have found that a gel made from banana peel extract (10-15%) helps burn wounds heal faster than the control group by making the skin thicker and reducing swelling in the area (Laloan *et al*., 2023).

These findings suggest that Goroho banana peel extract concentration significantly influences wound healing processes. The 3% concentration successfully demonstrated an optimal balance between healing effectiveness and extract efficiency, which could be a crucial consideration in developing subsequent gel extract formulations. The results highlight the potential of Goroho banana peel extract as a promising wound healing agent, with the 3% concentration emerging as the most effective treatment in this preliminary study. The superior wound healing efficacy of the 3% extract of Goroho banana peel compared to 1% and 5% concentrations can be attributed to several biological and pharmacological factors. At 3% concentration, the extract provides optimal levels of bioactive compounds (flavonoids, tannins, and saponins) for antioxidant, anti-inflammatory, and fibroblast stimulation effects without causing saturation or toxicity. Lower concentrations (1%) may not provide sufficient therapeutic effects, while higher concentrations (5%) might lead to saturation or inhibition due to potential toxic effects or reduced biological efficiency (Rizka *et al*., 2023). Research indicated that at 3% concentration, there is an ideal balance between the antioxidant activity of flavonoids and the anti-inflammatory effects of tannins, promoting re-epithelialization without interfering with the natural healing processes (Tamri *et al*., 2016). Additionally, the 3% concentration effectively inhibits pathogenic bacteria such as *Staphylococcus aureus* without disrupting the local microbiota balance that might occur at higher concentrations (Pangemanan *et al*., 2020). Therefore, for further testing, the spray gel formulation included 3% of Goroho banana (*M. acuminata* L.) peel extract

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Wound Healing Activity Test Using Spray Gel Formula

The primary objective of this research is to confirm and evaluate the effectiveness of the formulated preparation (spray gel) compared to direct extract with gel base usage. More specifically, this study aims to validate the formulation effectiveness by confirming the efficacy of Goroho banana peel extract at the optimal concentration (3%) in spray gel form. Although the 3% extract has proven effective in initial testing, the spray gel formulation might influence how stable it is, how well the active compounds are released, and how it interacts with skin tissue. According to recent research conducted by Rizka *et al*. (2023), using spray gels make it easier to apply and spread the treatment evenly on wounds, which can make it work better than just using pure extracts (Rizka *et al*., 2023). Furthermore, this study evaluates the physical and chemical stability of bioactive compounds (flavonoids, tannins, and saponins) after being formulated into a spray gel, as formulation can influence active compound release and potentially affecting wound healing effectiveness.

In this test, the data were first processed with a normality test, which showed that the data was not normally distributed, leading to the subsequent use of the Kruskal-Wallis test. The Kruskal-Wallis test revealed that among the five treatments (Bioplacenton, formula 1, formula A, formula B, and Formula AB), there were no significant differences in healing outcomes ($p > 0.05$). The Kruskal-Wallis data can be seen in Table 3.

The Kruskal-Wallis test results showed that there were no significant differences (P>0,05) between the treatment groups (Bioplacenton, formula 1, formula a, formula b, and formula ab) on days 1,3,6,9,and 12, leading to several important findings. The absence of significant differences indicates that all treatments demonstrated similar levels of effectiveness in wound healing, suggesting that your spray gel formulations (formulas 1, a, b, and ab) were equivalent in efficacy compared to the positive control (Bioplacenton), which is considered the gold standard in wound healing. The equivalent effectiveness between Goroho banana peel extract-based spray gel and Bioplacenton demonstrates that the spray gel can serve as an alternative pharmaceutical product for wound healing. This is a significant finding, as natural-based formulations like Goroho banana peel offer sustainability advantages and potentially lower side effects. Additionally, the lack of significant differences may indicate that formula modifications (formulas 1, a, b, and ab) did not produce substantial additional effects compared to Bioplacenton or the initial formulation, suggesting that the 3% concentration is already optimal, and formula modifications did not provide further improvements in wound healing effectiveness (Pradhan *et al*., 2023).

Evaluation of Spray Gel Formulation

The evaluation of Goroho banana peel extract spray gel formulation represents a crucial stage in pharmaceutical preparation development to ensure product quality and effectiveness. The evaluation process encompasses testing of physical characteristics such as viscosity, pH, and drying time, which play critical roles in determining formulation stability and acceptability. A thorough understanding of polymer concentration effects and their interactions is essential for formula optimization, aiming to produce a spray gel preparation that not only meets pharmaceutical requirements but also provides user convenience (Table 4). This comprehensive evaluation aims to achieve an optimal formula capable of facilitating the therapeutic effects of Goroho banana peel extract while maintaining desired physical characteristics.

The formulations exhibited consistent organoleptic properties across all four variants. Both Formula 1 and Formula A displayed a dark green color, a viscous consistency, and a characteristic Goroho banana peel aroma. Similarly, Formula B and Formula AB shared analogous organoleptic features, including the dark green color, viscous consistency, and the aroma of Goroho banana peel. The slight difference observed was that Formula B and AB demonstrated marginally higher viscosity values

Table 3. The Kruskal-Wallis test results

Kruskal-Wallis Test Results				
Day - 1	**Day - 3**	**Day - 6**	**Day - 9**	**Day - 12**
0.187	0.787	0.720	0.111	0.082

Table 4. Evaluation of spray gel formulation

Formula	Organoleptic	Homogeneity	Adhesiveness	pH	Viscosity	Spray Pattern Weight	Drying Time
1	Color : Dark Green, Consistency : Viscous. Odor: Characteristic Goroho banana peel aroma.	Homogeneous texture with no gritty particles	Adhere	5.13± 0.15	248.2 ± 12.5	0.13 ± 0.005	3.1 ± 0.01
A	Color : Dark Green, Consistency : Viscous. Odor: Characteristic Goroho banana peel aroma.	Homogeneous texture with no gritty particles	Adhere	4.36 ± 0.12	76.13 ± 2.54	0.121 ± 0.006	4.13 ± 0.02
B	Color : Dark Green, Consistency : Viscous. Odor: Characteristic Goroho banana peel aroma.	Homogeneous texture with no gritty particles	Adhere	5.13 ± 0.05	223.8 ± 7.6	0.128 ± 0.009	4.22 ± 0.05
AB	Color : Dark Green, Consistency : Viscous. Odor: Characteristic Goroho banana peel aroma.	Homogeneous texture with no gritty particles	Adhere	5.6 ± 0.1	241.2 ± 27.7	0.137 ± 0.005	2.53 ± 0.03

***X**±STD, standard deviation.

compared to Formula 1 and A. Overall, the organoleptic profiles of the spray gel formulations were uniform and aligned with the desired product specifications.

Regarding homogeneity, all four formulas were characterized as having a homogeneous texture with no gritty particles. This indicates that the manufacturing process was able to achieve a high degree of uniform blending and dispersion of the ingredients, resulting in smooth and consistent internal structures for the spray gels.

The adhesiveness, or the ability of the spray gel to adhere to the application surface, was also evaluated. All four formulations (Formula 1, A, B, and AB) were classified as "Adhere", demonstrating their capacity to remain in place after application and preventing potential runoff or dripping. The adhesive characteristic is essential for ensuring that the spray gel formulations are properly preserved on the skin for their intended purpose.

Overall, the data on organoleptic properties, homogeneity, and adhesiveness indicate that the development process was successful in producing spray gel formulations with consistent quality attributes and performance characteristics that meet the target specifications.

The pH evaluation of the spray gel preparations showed a pH range of 4.36-5.6. Formula A had the lowest pH of 4.36±0.12, while formula AB showed the highest pH of 5.6±0.1. The pH values obtained from all four formulas remained within the acceptable pH range for topical preparations of 4.5-6.5, ensuring their safety for skin use without inducing irritation. The variations in pH levels among the formulations were likely affected by the interactions of the components utilized in the formulation.

Viscosity testing revealed significant variations between formulas. Formula A had the lowest viscosity of 76.13±2.54, while formula 1 showed the highest viscosity of 248.2±12.5. These viscosity differences can affect the ease of application of the spray gel preparation on the skin. Viscosity that is too low can cause the preparation to be too runny and flow easily, while viscosity that is too high can impede the

spraying process. Formulas B and AB showed moderate viscosity values that were still acceptable for spray gel preparations.

The evaluation of spray pattern weight showed relatively uniform results between formulas ranging from 0.121 to 0.137 g. Formula 1 had a spray pattern weight of 0.13±0.005 g, formula A of 0.121±0.006 g, formula B of 0.128±0.009 g, and formula AB of 0.137±0.005 g. This uniformity in spray pattern weight indicates consistency in the delivery of the preparation when sprayed, which is important for ensuring proper dosage with each use.

The drying time of the spray gel preparations varied from 2.53 to 4.22 minutes. Formula AB had the fastest drying time of 2.53±0.03 minutes, while formula A had the longest drying time of 4.13±0.02 minutes. These differences in drying time can be influenced by the composition of ingredients and the viscosity of the preparation. Faster drying times are generally preferred as they provide better user comfort. All formulas demonstrated acceptable drying times for spray gel preparations, although formula AB showed more optimal drying characteristics.

Physical Properties Response

Viscosity

The Viscosity Response can be observed from the factorial design equation for viscosity response as follows:

$$Y = 197.4 - 36.60X_1 + 35.23X_2 + 47.43X_1X_2$$

Variable Y represents the Viscosity response where X_1 is Carbopol and X_2 is hydroxypropyl methylcellulose (HPMC). Meanwhile, X_1X_2 represents the interaction between carbopol and HPMC factors. The factorial design equation above shows the viscosity calculation based on the amount used of each factor, namely carbopol and HPMC. The effects and p-values of carbopol and HPMC and their interactions on viscosity are presented in Table 5.

Based on Table 5, the effects of Carbopol, hydroxypropyl methylcellulose (HPMC), and their interaction on viscosity response demonstrated distinct patterns. Carbopol had a significant negative effect (-72.201) with a contribution of 28.95% ($p<0.0001$), indicating that increasing Carbopol concentration resulted in decreased viscosity. Meanwhile, HPMC showed a positive effect (70.465) with a 24.11% contribution, suggesting that higher HPMC concentrations led to increased viscosity. Notably, the interaction between Carbopol and HPMC demonstrated the most dominant effect (94.863) with a 43.71% contribution, revealing a synergistic relationship where the combination of both polymers significantly enhanced the viscosity response. This interaction effect proved to be more influential than the individual effects of either polymer alone, highlighting the importance of considering polymer combinations in formulation development.

Molecular mechanisms and polymer interactions explain the different effects of Carbopol and HPMC on viscosity. Carbopol shows a significant negative effect (-72.201, 28.95% contribution) due to its concentration-sensitive structural characteristics. When Carbopol is used in high amounts, its polymer chains can get too tangled up, leading to the collapse of its three-dimensional structure and the reduction of viscosity.

Conversely, HPMC provides a positive effect (70.465, 24.11% contribution) through hydrophilic gel formation mechanisms. Increased HPMC concentration results in stronger gel matrices through hydrogen bonding and hydrophobic interactions between its polymer chains, contributing to increased system viscosity (Shafiei *et al.*, 2018).

Table 5. Effect of Carbopol, HPMC and their interactions on viscosity response

Factors	Effects	% Contribution	*P*- value	*P* value model
Carbopol	-72.201	28.95	<0.0001	<0.0001 (Significant)
HPMC	70.465	24.11		
Interaction	94.863	43.71		

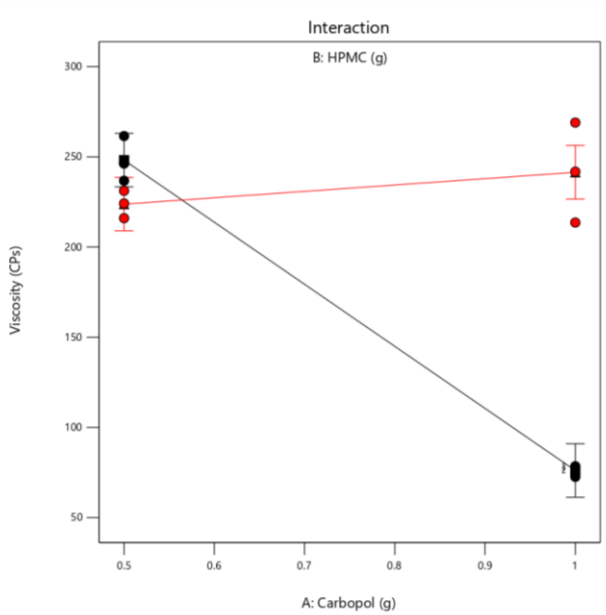

Figure 3. The Interaction of Carbopol and HPMC on Viscosity Response of Goroho Banana Peel Spray Gel.

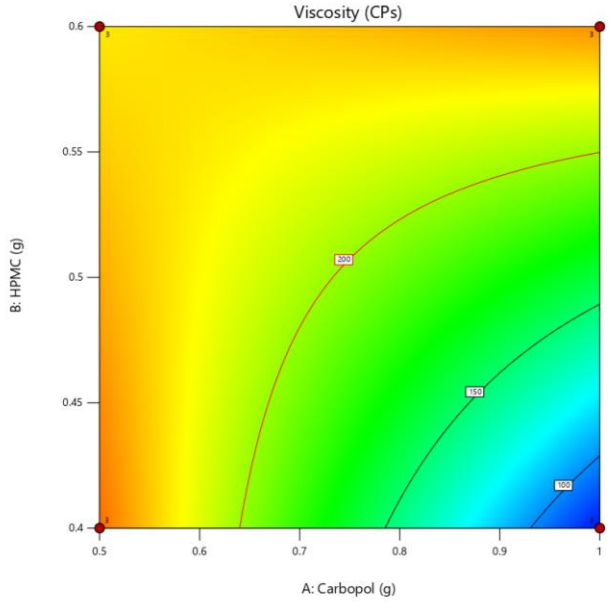

Figure 4. Contour Plot of Goroho Banana Peel Spray Gel Viscosity Response.

The dominant interaction between both polymers (94.863, 43.71% contribution) demonstrates a strong synergistic effect, where HPMC plays a role in stabilizing the Carbopol network. HPMC can form an interpenetrating network with Carbopol, creating a more complex and stable structure. HPMC molecules help prevent excessive Carbopol chain entanglement and maintain three-dimensional network expansion, resulting in greater viscosity enhancement compared to the individual effects of each polymer. This phenomenon explains why the interaction of both polymers provides the largest contribution to system viscosity (Sheshala *et al*., 2019).

The study of how Carbopol and HPMC affect viscosity showed different results depending on their concentrations (Figure 3). At a low HPMC concentration of 0.4 g, raising the Carbopol concentration from 0.5 g to 1.0 g led to a big drop in viscosity. Conversely, at high HPMC concentration (0.6 g), increasing Carbopol

concentration led to a slight but significant increase in viscosity. The significant interaction between these two polymers is indicated by the crossing lines in the interaction graph, where high HPMC concentration was able to maintain and even increase system viscosity when Carbopol concentration was increased. This result indicates that HPMC plays a crucial role in moderating Carbopol's effect on viscosity and demonstrates that spray gel viscosity optimization is highly dependent on selecting the appropriate concentrations of both polymers.

The contour plot interpretation (Figure 4) reveals a complex relationship between Carbopol and HPMC in influencing spray gel viscosity. Analysis results show that HPMC plays a crucial role as the primary controller of system viscosity, where high HPMC concentration (0.6 g) consistently produces higher viscosity (~269 CPs) regardless of Carbopol concentration variations. On the other hand, using a small amount of HPMC (0.4 g) with a large amount of Carbopol (1.0 g) leads to the lowest viscosity (~72.6 CPs), indicating an antagonistic interaction under these conditions. The curved contour lines confirm significant interaction between both polymers, with an optimal prediction point at Carbopol concentration of 0.617622 g and HPMC of 0.414602 g yielding a viscosity of 209.189 CPs. These findings have important implications for formulation development, where viscosity optimization can be achieved through careful adjustment of HPMC concentration as the dominant factor while considering the moderating effect of Carbopol. This result emphasizes the importance of a systematic approach in polymer concentration selection to achieve desired viscosity characteristics in spray gel formulation.

pH

The pH Response can be observed from the factorial design equation for pH response as follows:

$$Y = 197.4 - 36.60X_1 + 35.23X_2 + 47.43X_1X_2$$

Variable Y represents the pH response where X1 is Carbopol and X2 is HPMC. Meanwhile, X1X2 represents the interaction between carbopol and HPMC factors. The factorial design equation above shows the pH calculation based on the amount used of each factor, namely carbopol and HPMC. The effects and p-values of carbopol and HPMC and their interactions on viscosity are presented in Table 6.

The factorial design equation and the data show significant patterns in how Carbopol HPMC, and their interaction affect pH response. Carbopol exhibits a negative effect (-0.15) with a 2.733% contribution and p-value of 0.0667, indicating that increasing Carbopol concentration tends to decrease pH, although the effect is relatively small. Meanwhile, HPMC shows a larger positive effect (0.616667) with a 46.2032% contribution and *p*-value <0.0001, indicating a highly significant influence on pH increase. The interaction between both factors also demonstrates a positive effect (0.616667) with an equally substantial contribution of 46.2032% and *p*-value <0.0001, confirming strong synergy between both polymers in influencing pH. The overall model shows high significance (model *p*-value <0.0001), confirming that the observed pH changes result from the systematic influences of both factors and their interaction.

This phenomenon can be explained through the chemical characteristics and interaction mechanisms of both polymers. Carbopol shows a negative effect on pH due to its carboxylic acid (COOH) properties. When Carbopol disperses in water, the carboxylate groups undergo partial dissociation, releasing H+ ions that cause pH reduction. HPMC's positive effect can also be attributed to its ability to form a protective layer around Carbopol molecules, which may reduce carboxylate group dissociation. The strong interaction between

Table 6. Effect of carbopol, HPMC and their interactions on pH response

Factors	Effects	% Contribution	*P*- value	*P* value model
Carbopol	-0.15	2.733	0.0667	<0.0001 (Significant)
HPMC	0.616667	46.2032	<0.0001	
Interaction	0.616667	46.2032	<0.0001	

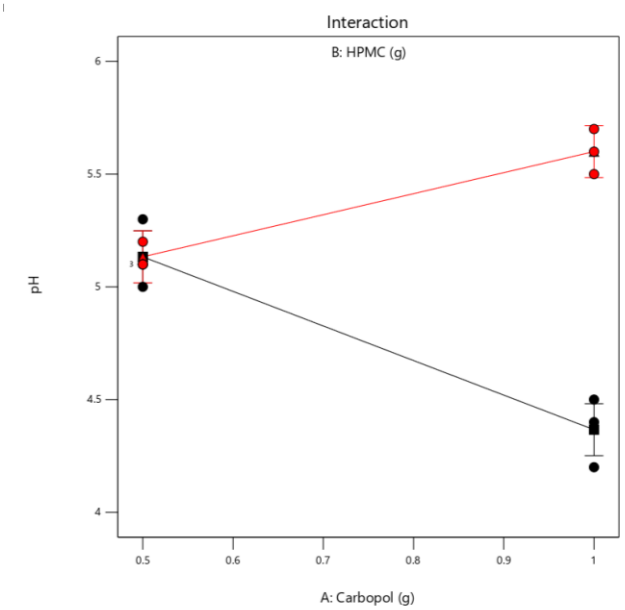

Figure 5. The Interaction of Carbopol and HPMC on pH Response of Goroho Banana Peel Spray Gel.

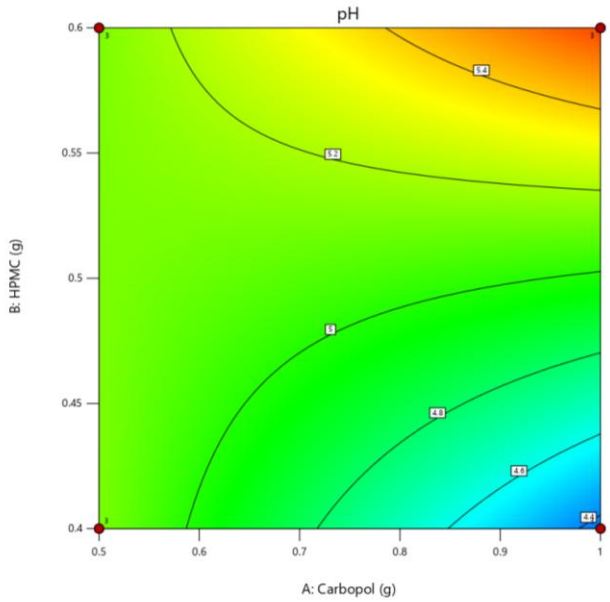

Figure 6. Contour Plot of Goroho Banana Peel Spray Gel pH Response.

both polymers (46.2032% contribution) indicates a synergistic effect, where HPMC can moderate Carbopol's acidic properties through the formation of complex interpenetrating polymer networks. This results in a more stable system with a higher pH compared to when Carbopol is used alone (Zhang *et al.*, 2016).

The interaction graph demonstrates the influence of Carbopol (0.5-1.0 g) and HPMC (0.4-0.6 g) on pH response (Figure 5). At a low HPMC concentration (0.4 g) shown by the black line, increasing Carbopol concentration from 0.5 g to 1.0 g causes a significant pH decrease. Conversely, at a high HPMC concentration (0.6 g) shown by the red line, increasing Carbopol concentration results in a significant pH increase. The intersection of these lines indicates a significant interaction between both polymers in

influencing system pH. HPMC at high concentration can neutralize the acidifying effect of Carbopol, even resulting in a pH increase. This demonstrates HPMC's important role in controlling the pH of the spray gel system.

Drying Time

The Drying Time Response can be observed from the factorial design equation for Drying Time response as follows:

$$Y = 35.2 - 0.1900X_1 + 0.1433X_2 + 0.6583X_1X_2$$

Variable Y represents the Drying Time response where X1 is Carbopol and X2 is HPMC. Meanwhile, X1X2 represents the interaction between carbopol and HPMC factors. The factorial design equation above shows the Drying Time calculation based on the amount used of each factor, namely carbopol and HPMC. The effects and p-values of carbopol and HPMC and their interactions on viscosity are presented in Table 7.

The analysis of drying time effects reveals an interesting pattern where all three factors demonstrate negative effects with varying degrees of contribution. Carbopol shows a negative effect (-0.38) with a 7.35313% contribution and $p<0.0001$, indicating that increasing Carbopol concentration accelerates drying time. HPMC also exhibits a negative effect (-0.286667) with a 4.18465% contribution and $p<0.0001$, indicating that higher HPMC concentrations accelerate the drying process. The interaction between both polymers shows the largest negative effect (-1.31667) with a dominant contribution of 88.2789% and $p<0.0001$, indicating that the simultaneous use of both polymers considerably influences the drying rate of the spray gel.

The negative effects on drying time can be explained through molecular mechanisms and physicochemical characteristics of the formula components. Carbopol contributes to accelerated drying (-0.38) due to its ability to form three-dimensional network structures that facilitate uniform distribution of volatile components. HPMC also contributes to drying acceleration (-0.286667) through the formation of thin and uniform films, facilitating solvent evaporation. The interaction between both polymers shows a dominant synergistic effect (-1.31667) in accelerating drying, where the complex interpolymer network creates a structure that enables more efficient solvent evaporation (Begum *et al*., 2021).

The inclusion of 20% alcohol at 95% concentrations in the formulation significantly enhances drying times due to several factors: (1) alcohol's higher vapor pressure compared to water accelerates the evaporation process, (2) alcohol helps to reduce surface tension, resulting in better spreading and thinner spray layers, (3) the volatile characteristic of alcohol promote fast film formation and (4) alcohol assists in the solubilization of formula components, resulting in more homogeneous distribution and uniform drying (Dohrn *et al*., 2020).

The interaction graph demonstrates distinct relationships between Carbopol and HPMC in influencing the spray gel drying time. At a low concentration of HPMC (0.4 g), as indicated by the black line, an increase in Carbopol concentration result in significant increase drying time. Conversely, at high HPMC concentration (0.6 g) shown by the red line, higher Carbopol concentration results in a significant decrease in drying time. The intersection of these lines indicates a strong interaction between both polymers in influencing the system's drying time, where the effect of Carbopol on drying time strongly depends on the HPMC concentration used.

The molecular interaction mechanism between the polymers explain this phenomenon and their role in the spray gel system. At low HPMC concentration, increasing Carbopol concentration leads to longer drying times because Carbopol forms a thicker gel network with high water-binding capacity, thus inhibiting solvent evaporation.

Table 7. Effect of carbopol, HPMC and their interactions drying time response

Factors	Effects	% Contribution	*P*- value	*P* value model
Carbopol	-0.38	7.35313	<0.0001	<0.0001 (Significant)
HPMC	-0.286667	4.18465	<0.0001	
Interaction	-1.31667	88.2789	<0.0001	

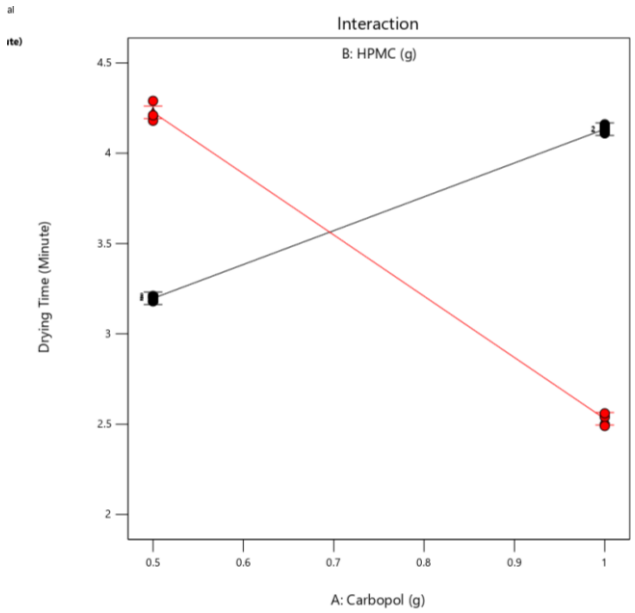

Figure 7. The Interaction of Carbopol and HPMC on pH Response of Goroho Banana Peel Spray Gel.

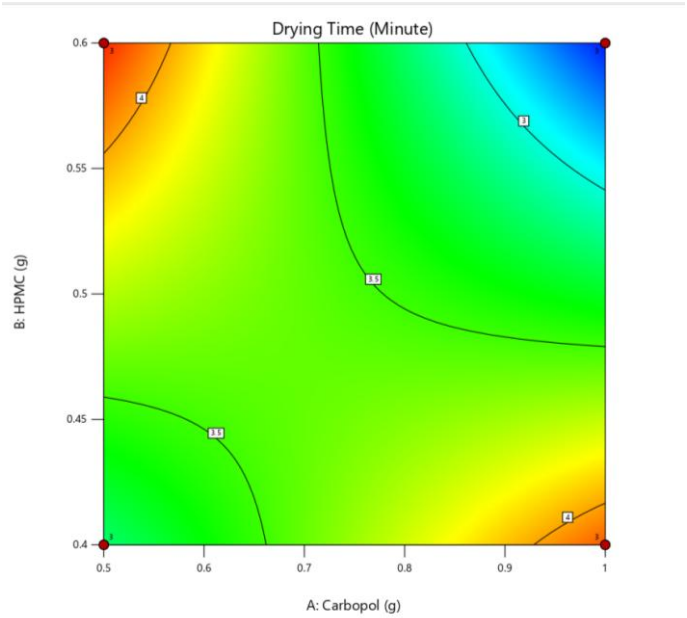

Figure 8. Contour Plot of Goroho Banana Peel Spray Gel Drying Time Response.

Conversely, at high HPMC concentration, increasing Carbopol concentration accelerates drying time due to the formation of complex interpolymer networks between HPMC and Carbopol. This interaction results in a more organized film structure with uniform solvent distribution, facilitating more efficient evaporation (Begum *et al*., 2021). Additionally, the presence of 95% alcohol in the formula plays a crucial role in accelerating the drying process through increased evaporation rate and reduced surface tension, resulting in thinner spray layers and faster drying.

The contour plot analysis illustrates the relationship between Carbopol and HPMC regarding the drying time response of spray gel. The visualization with color gradients from blue to orange provides insights into drying time distribution, with blue areas representing short drying periods, green areas representing

medium drying times, and orange parts representing longer drying times. At low HPMC concentration, increasing Carbopol concentration results in orange areas in the lower right, indicating longer drying times. Conversely, at high HPMC concentrations, blue areas are observed in the upper right, indicating faster drying times despite increased Carbopol concentration. The curved contour lines indicates a significant interaction between the two polymers, with HPMC being essential in regulating the drying time of the spray gel system.

The optimization of Goroho banana peel extract spray gel formula using Design Expert generated 100 potential formula solutions with perfect desirability values (1.000). Figure 9 presents the top five solutions from the optimization results. The optimal formula (solution number 1) contains 0.670% Carbopol 940 and 0.517% HPMC, with predicted physical characteristics viscosity of 213.229 cPs, pH at 5.119, and drying time of 3.594 minutes. These optimization results demonstrate a good balance between the concentrations of both polymers, where this combination produces a preparation with appropriate viscosity for spray gel (200-300 cPs), pH approaching the physiological range of skin (4.5-6.5), and an optimal drying time (<5 minutes). This optimal formula was selected as it meets all required physical parameters with maximum desirability value, indicating perfect optimization in meeting the established criteria for spray gel preparation.

Irritation Testing

Irritation testing of spray gel formulations is a crucial step in formula development to ensure product safety before human use. The Hen's Egg Test-Chorioallantoic Membrane (HET-CAM) method is identified as a valid *in vitro* alternative to the traditional Draize test conducted on animals. This method utilizes the chorioallantoic membrane of chicken eggs, which shares similar characteristics with human mucous membranes, including good vascularization for detecting blood vessel changes due to irritation. In its implementation, The HET-CAM method assesses three primary parameters: hemorrhage, lysis (blood vessel damage), and coagulation (protein clumping), which can be quantified to determine irritation scores. The advantages of this method include relatively simple procedures, short observation time (15-20 minutes), more economical costs compared to in vivo testing, and compliance with the 3R principles (Replacement, Reduction, Refinement) in testing. Specifically, for spray preparations, this method enables the evaluation of direct spray effects on membranes and assessment of preparation distribution, making it highly relevant for evaluating the irritation potential of topically applied preparations. Test results using the HET-CAM method provide comprehensive information regarding the safety level of the preparation, its potential for irritation, and its appropriateness for human use, serving as valuable supporting data in product safety documentation (Rivero *et al*., 2021).

Table 8. Optimization Results of Goroho Banana Peel Extract Spray Gel Formula Using Design Expert Software.

No.	Carbopol	HMPC	Viscosity	pH	Drying Time	Desirability	Desirablity (w/o intervals)	
1	**0.670**	**0.517**	**213.229**	**5.119**	**3.594**	**1.000**	**1.000**	**Selected**
2	0.500	0.400	248.203	5.133	3.197	1.000	1.000	
3	1.000	0.600	241.467	5.600	2.530	1.000	1.000	
4	0.500	0.600	223.800	5.133	4.227	1.000	1.000	
5	0.858	0.593	232.573	5.437	3.042	1.000	1.000	
6	0.562	0.591	226.031	5.185	3.985	1.000	1.000	
7	0.870	0.587	229.352	5.419	3.031	1.000	1.000	
8	0.700	0.538	215.018	5.168	3.556	1.000	1.000	
9	0.859	0.573	221.418	5.349	3.123	1.000	1.000	
10	0.645	0.535	218.924	5.152	3.647	1.000	1.000	
11	0.710	0.584	226.760	5.287	3.521	1.000	1.000	
12	0.769	0.563	218.917	5.262	3.385	1.000	1.000	

Table 9. Irritation testing using HET-CAM results

Group	HET-CAM Irritation Score	Response Category
Lactic Acid	9.71	Severe Irritation
Aquadest	0	Negligible
Formula 1	3.8	Slight Irritation
Formula A	3.5	Slight Irritation
Formula B	2.5	Slight Irritation
Formula Ab	3.2	Slight Irritation

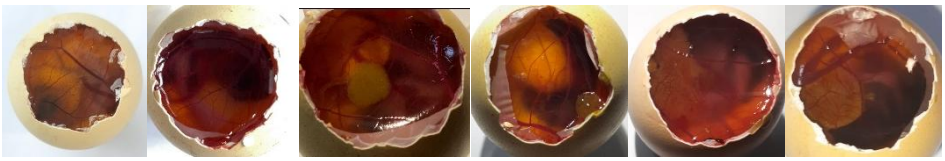

Figure 9. HET-CAM Irritation Test (F1: Formula 1, FA: Formula A, FB: Formula B, FAB: Formula AB).

The irritation test using the HET-CAM method was conducted using a total of 36 eggs divided into 6 treatment groups, with each group consisting of 6 eggs as replicates (Figure 9). Lactic acid, used as a positive control, showed the highest irritation score of 9.71 with a strong irritation response category, while aquadest, as a negative control showed an irritation score of 0 with a very mild category. In testing the spray gel formulations, formula 1 showed a score of 3.8, formula A showed 3.5, formula B showed 2.5, and formula AB showed 3.2, with all formulations falling within the mild irritation category. The results indicate that all developed spray gel formulations show relatively safe irritation levels, with formula B showing the lowest irritation level among the tested formulations. The findings indicate that all developed formulations comply with safety.

The HET-CAM irritation test results showed varying scores across different treatment groups. The positive control using lactic acid produced the highest irritation score of 9.71 (strong irritation) due to its acidic nature, which can cause protein denaturation and direct cell membrane damage to the chorioallantoic membrane, while aquadest, as a negative control showed a score of 0 (very mild) due to its isotonic properties. All developed spray gel formulations demonstrated irritation scores in the mild category, ranging from 2.5 to 3.8, where formula B showed the lowest irritation score (2.5), followed by formula AB (3.2), formula A (3.5), and formula 1 (3.8).

The results showing mild irritation category across all spray gel formulations can be explained through optimization of composition and physicochemical characteristics of the preparation. The use of combined gel bases, Carbopol 940 (0.5-1%) and HPMC (0.4-0.6%) significantly influenced irritation levels, where formula B, with the composition of Carbopol 0.5% and HPMC 0.6%, produced a more biocompatible gel matrix. Additional components, such as propylene glycol 15% as a humectant, a combination of methyl paraben (0.02%) and propyl paraben (0.18%) as preservatives in minimal concentrations, and ethanol 96% (20%) as solvent, were within concentration ranges tolerable by biological membranes. The optimization of the ratio between Carbopol and HPMC proved successful in producing spray gel preparations with minimal irritation levels while maintaining the desired physical characteristics.

CONCLUSIONS

Goroho banana (*Musa acuminata* L.) peel extract has been successfully formulated into spray gel preparations with optimal characteristics. The preliminary study established 3% as the optimal extract concentration, demonstrating comparable wound healing efficacy to Bioplacenton with the smallest wound diameter (0.73 cm) after 12 days of treatment. The factorial design optimization yielded Formula B (Carbopol 0.5% and HPMC 0.6%) as the optimal formulation, exhibiting desirable physical characteristics including viscosity (223.8 ± 7.6 cPs), pH (5.13 ± 0.05), and drying time (4.22 ± 0.05 minutes). The interaction between Carbopol and HPMC significantly influenced the preparation's properties, particularly affecting drying time (88.27% contribution). HET-CAM testing confirmed the safety profile of all formulations,

with Formula B showing the lowest irritation score (2.5). Wound healing assessment demonstrated no significant differences between the spray gel formulations and Bioplacenton ($p>0.05$), indicating comparable therapeutic efficacy. These findings suggest that the developed spray gel formulation of Goroho banana peel extract represents a promising alternative for wound healing applications, combining the advantages of natural ingredients with pharmaceutical acceptability.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest in this research. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors confirm that they had full access to all data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis. No external sponsors or organizations had any involvement in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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